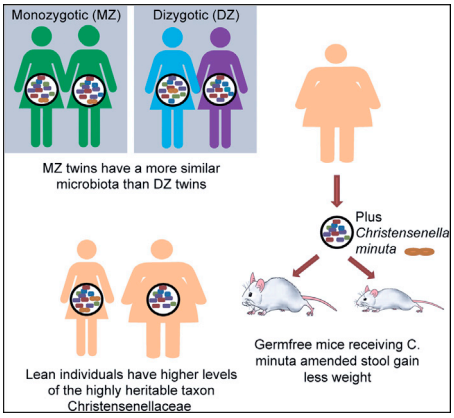
In This Issue

Cell



Two-rrific Microbiota against Obesity

PAGE 789

In a large twin study of the human gut microbiome, Goodrich et al. show that the abundance of certain gut microbes is heritable. The most heritable taxon, the family Christensenellaceae, is more abundant in lean individuals, counteracts the metabolic effects of an obese-associated microbiota, and confers resistance to weight gain in mice.

Neuron Speaks Analog and Digital

PAGE 751

Li et al. report that a single interneuron in the nematode *C. elegans* regulates two distinct motor outputs by controlling circuits that function in an analog- and digital-like manner, respectively. Both circuits employ the neurotransmitter acetylcholine (ACh) but utilize different postsynaptic ACh receptors to control locomotion speed or direction switching.

Human Oligodendrocytes Never Retire

PAGE 766

Studies in rodents have suggested that newly generated oligodendrocytes contribute to myelination, which mediates neural plasticity. Yeung et al. report that, in human white matter, the oligodendrocyte population is remarkably static, and oligodendrocyte generation could not account for the increase in myelin volume seen in response to experience in humans. The findings indicate that myelin remodeling in human brains may be independent of cell turnover and mainly carried out by mature oligodendrocytes.

Ordered Cell Division in the Brain

PAGE 775

Gao et al. track progenitor division pattern and potential in vivo at single-cell resolution in mammalian neocortex. They find that individual radial glial progenitors divide a defined number of times to produce excitatory neurons that initially enter the deep layers of the neocortex before populating the more superficial layers. A constant fraction of these neurons go on to produce glia, maintaining the balance between the two cell types.

Human T Cells on the Map

PAGE 814

Thome et al. report a multidimensional, quantitative analysis of T cell subsets in blood, lymphoid, and multiple mucosal tissues obtained from healthy organ donors, spanning six decades of life. By mapping the different T cell subsets and compartments, they show that T cell homeostasis driven by cytokine or TCR-mediated signals is different in $CD4^+$ or $CD8^+$ T cell lineages, varies with their differentiation stage and tissue localization, and cannot be inferred from blood.

No Immunity for Old Flies

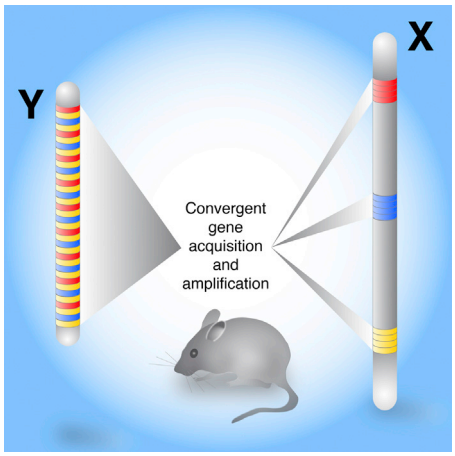
PAGE 829

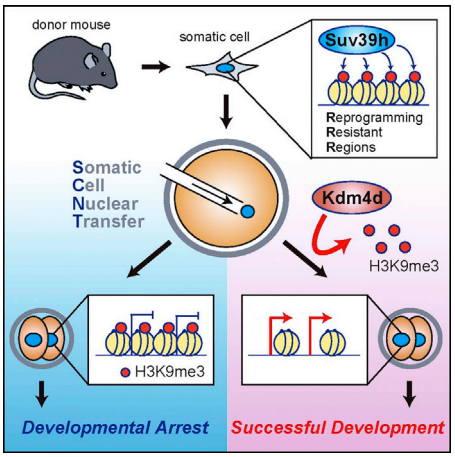
Aging is associated with several physiological changes, including a functional decline in immune function known as immunosenescence. Exploring the molecular underpinnings of immunosenescence, Chen et al. find that aging is marked by the loss of lamin B in the fat body, a major immune organ in flies, and this results in systemic inflammation, gut hyperplasia, and immune repression, revealing that molecular crosstalk between tissues is a critical contributing factor.

Y Break the Mold, Mouse?

PAGE 800

Soh et al. report that the murine Y chromosome is strikingly distinct from previously characterized mammalian/primate Y chromosomes. It is almost entirely euchromatic, including three families of massively amplified genes absent from primate Y chromosomes, but also amplified on the mouse X chromosome. The patterns of gene amplification suggest competition between the X and Y chromosomes as a major evolutionary driving force in mouse sex chromosome evolution.





Sweeping Away Methylation for Clean Cloning

PAGE 884

Animal cloning by somatic cell nuclear transfer (SCNT) is inefficient as few embryos reach the blastocyst stage. Comparative transcriptome and epigenome analysis by Matoba et al. reveals that H3K9me3 in the mouse somatic cell genome prevents transcriptional activation of associated genomic regions following SCNT leading to developmental arrest. Removal of H3K9me3 in donor somatic cells restores transcriptional activation of the transferred somatic genome and greatly improves developmental efficiency.

Noncanonical Metastasis

PAGE 844

Wnt signaling is known to control distinct aspects of tumorigenesis. Here, Gujral et al. find that a noncanonical pathway mediated by Fzd2 and Wnt5 can directly promote epithelial-mesenchymal transition, tumor growth, and metastasis. Blocking Fzd2 reduces metastatic tumor growth in vivo—hence, it may be a viable therapeutic option.

Fine Motor Control

PAGE 857

Bhabha et al. report X-ray and EM structures of the yeast dynein motor domain bound to different ATP analogues, allowing them to model the conformational transitions during a complete motility cycle. These results reveal distinct roles for dynein's two critical ATPase sites and reveal an unanticipated regulatory role for the linker region in controlling movement.

Guidance for PRC2

PAGE 869

Long noncoding RNAs (lncRNAs) have emerged as key epigenetic regulators that function together with chromatin regulatory complexes, including Polycomb Repressive Complex 2 (PRC2). Sarma et al. report that the chromatin remodeling protein ATRX anchors PRC2 binding to Xist RNA. Additionally, ATRX regulates the specific targeting of PRC2 to chromatin on a genome-wide scale, demonstrating a new functional contribution on both X chromosomes and autosomes.

Clear-Cut Solution for Whole-Body Imaging

PAGE 896 and PAGE 911

Understanding whole-organ and whole-organism physiology demands effective imaging techniques. Two papers in this issue of *Cell* advance the ability to clear mammalian tissues for microscopy. Renier et al. present iDisco, enabling deep immunolabeling and volume imaging of fine anatomical structures in large, cleared tissues and facilitating insights into neuronal generation. Tainaka et al. show that their previously CUBIC technique for brain imaging is effective for whole-body clearing due to the chemical extraction of heme and other chromophores enabling full-body imaging with single-cell resolution, including the distinction between healthy and pathological states.

Giving Synthetic Biology a Toe

PAGE 925

Green et al. describe a new class of RNA-based devices called toehold switches that can be used for highly dynamic regulation of gene expression. Dozens of toehold switches can operate independently of one another in a cell, allowing rapid construction of complex synthetic gene networks.

A Paper Route for Synthetic Biology

PAGE 940

Pardee et al. present a paper-based platform that provides a new venue for synthetic biologists to operate. This cell-free system, freeze dried onto paper, enables rapid prototyping of complex gene circuits and programmable in vitro diagnostics, including glucose and strain-specific Ebola virus sensors. The low cost of the technology allows its application outside of the lab and provides a much-needed medium for the safe use of engineered gene circuits in clinic, global health, industry, research, and education.